VEGF optimizes the formation of tissue-engineered small intestine.

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Authors: Jamil A Matthews, Frederic G Sala, Allison L Speer, David Warburton, Tracy C Grikscheit

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Public Summary:
Increasing the amount of VEGF, a growth factor, available when tissue engineered intestine is forming improves growth of the engineered intestine by several measures. This could be helpful for moving toward a human therapy.

Scientific Abstract:
AIM: To determine the effect of VEGF overexpression on tissue-engineered small intestine (TESI) formation. MATERIALS & METHODS: Organoid units were isolated from the intestines of 2-week-old transgenic mouse pups capable of inducible, ubiquitous VEGF overexpression (CMV-Cre/rtTA/tet(0)-VEGF) and implanted into nonobese diabetic/severe combined immunodeficiency mice. Resulting TESI were explanted at 2 and 4 weeks, and studied by histology, tissue ELISA and immunofluorescence. RESULTS: At 2 weeks postimplantation, the TESI mucosa from the VEGF overexpression group formed rudimentary villi and more crypts compared with controls, which demonstrated a flat epithelium with few crypts and no villi. At 4 weeks postimplantation, the TESI from the VEGF overexpression group was larger and significantly heavier than controls. Within the mucosa, the villus height and crypt depth was significantly longer, contained a greater percentage of proliferating crypt epithelial cells and consisted of all four terminally differentiated epithelial cell types. There was also a significant increase in the capillary density within the submucosa. CONCLUSIONS: Overexpression of VEGF optimizes the formation of TESI by increasing the submucosal capillary density, crypt epithelial proliferation and the rate of mucosa formation. A larger construct with increased villus and crypt height was noted after 4 weeks in vivo.